

IN THE CLAIMS:

Applicants, pursuant 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Currently amended) A method for diagnosis or prognosis of esophageal diagnosing cancer or esophageal cancer-related conditions ~~from tissue samples~~, comprising:

(a) obtaining a esophageal tissue sample comprising genomic DNA ~~from a test tissue or region to be diagnosed~~;

(b) performing a methylation assay of the tissue sample, wherein the methylation assay determines the methylation state of at least one genomic CpG sequence ~~sequences~~, wherein the genomic CpG sequence ~~is sequences~~ are located within the MYOD1 gene ~~at least one gene sequence selected from the group consisting of~~ *APC, ARF, CALCA, CDH1, CDKN2A, CDKN2B, ESRI, GSTP1, HIC1, MGMT, MLH1, MYOD1, RBI, TGFBR2, THBS1, TIMP3, CTNNB1, PTGS2, TYMS* and *MTHFR*, ~~and combinations thereof~~; and

(c) ~~determining, making a diagnostic or prognostic prediction of the cancer based, at least in part, upon the methylation state of the~~ at least one genomic CpG sequence ~~sequences~~, a diagnosis or prognosis of esophageal cancer or an esophageal cancer-related condition.

2. (Currently amended) The method of claim 1, wherein the at least one genomic CpG sequence ~~sequences~~ located within the MYOD1 gene ~~at least one gene sequence selected from the group consisting of~~ *APC, ARF, CALCA, CDH1, CDKN2A, CDKN2B, ESRI, GSTP1, HIC1, MGMT, MLH1, MYOD1, RBI, TGFBR2, THBS1, TIMP3, CTNNB1, PTGS2* and *TYMS*, correspond to genomic CpG sequences of a CpG island ~~islands~~.

3. (Currently amended) The method of claim 1, wherein the MYOD1 ~~*APC, ARF, CALCA, CDH1, CDKN2A, CDKN2B, ESRI, GSTP1, HIC1, MGMT, MLH1, MYOD1, RBI, TGFBR2, THBS1, TIMP3, CTNNB1, PTGS2, TYMS*~~ gene sequences are those defined by the specific oligonucleotide primers and probes corresponding to SEQ ID NOS:7-9 ~~SEQ ID Nos:1-60, 64 and 65~~, as listed in TABLE II, or portions thereof.

4. (Currently amended) The method of claim 2 wherein the CpG island ~~is islands~~ are located within the promoter region ~~regions~~ of the MYOD1 gene ~~one or more of the~~ *APC, ARF,*

~~CALCA, CDH1, CDKN2A, CDKN2B, ESRI, GSTP1, HIC1, MGMT, MLH1, MYOD1, RB1, TGFB2, THBS1, TIMP3, CTNNB1, PTGS2 and TYMS genes.~~

5. (Currently amended) The method of claim 2, wherein the MYOD1 gene sequence corresponds ~~APC, ARF, CALCA, CDH1, CDKN2A, CDKN2B, ESRI, GSTP1, HIC1, MGMT, MLH1, MYOD1, RB1, TGFB2, THBS1, TIMP3, CTNNB1, PTGS2, and TYMS gene sequences~~ correspond to any CpG island sequences associated with the sequences defined by the specific oligonucleotide primers and probes corresponding to SEQ ID NOS:7-9 ~~SEQ ID NOS:1-54, 58-60, 64 and 65~~, as listed in TABLE II, or portions thereof, and wherein the associated CpG island sequences are those contiguous sequences of genomic DNA that encompass at least one nucleotide of the sequences defined by the specific oligonucleotide primers and probes corresponding to SEQ ID NOS:7-9 ~~SEQ ID NOS:1-54, 58-60, 64 and 65~~, and satisfy the criteria of having both a frequency of CpG dinucleotides corresponding to an Observed/Expected Ratio >0.6, and a GC Content >0.5.

6. (Currently amended) The method of claim 1, comprising determining the methylation state of a plurality of genomic CpG sequence located within the MYOD1 gene ~~wherein the genomic CpG sequences are located within at least one gene sequence selected from the group consisting of APC, CDKN2A, MYOD1, CALCA, ESRI, MGMT and TIMP3, and combinations thereof.~~

7. (Currently amended) The method of claim 6, wherein the genomic CpG sequences ~~located within at least one gene sequence selected from the group consisting of APC, CDKN2A, MYOD1, CALCA, ESRI, MGMT and TIMP3~~, correspond to genomic CpG sequences of a CpG island islands.

8. (Currently amended) The method of claim 6, wherein at least one of the CpG sequences is defined ~~the APC, CDKN2A, MYOD1, CALCA, ESRI, MGMT and TIMP3 gene sequences are those defined~~ by the specific oligonucleotide primers and probes corresponding to ~~SEQ ID NOS:19-21, SEQ ID NOS:1-3, SEQ ID NOS:7-9, SEQ ID NOS:10-12, SEQ ID NOS:4-6, SEQ ID NOS:16-18 and SEQ ID NOS:13-15, respectively~~, as listed in TABLE II.

9. (Currently amended) The method of claim 7 wherein the CpG ~~island is~~ islands are located within the promoter ~~region~~ regions of the MYOD1 gene ~~one or more of the APC, CDKN2A, MYOD1, CALCA, ESRI, MGMT and TIMP3 genes.~~

10. (Currently amended) The method of claim 7 wherein the CpG sequences are within APC, CDKN2A, MYOD1, CALCA, ESRI, MGMT and TIMP3 gene sequences ~~correspond to any CpG island sequence~~ ~~sequences~~ associated with the sequences defined by the specific oligonucleotide primers and probes corresponding to ~~SEQ ID NOs:19-21, SEQ ID NOs:1-3, SEQ ID NOs:7-9, SEQ ID NOs:10-12, SEQ ID NOs:4-6, SEQ ID NOs:16-18 and SEQ ID NOs:13-15, respectively,~~ as listed in TABLE II, or portions thereof, and wherein the associated CpG island sequences are those contiguous sequences of genomic DNA that encompass at least one nucleotide of the sequences defined by the specific oligonucleotide primers and probes corresponding to ~~SEQ ID NOs:19-21, SEQ ID NOs:1-3, SEQ ID NOs:7-9, SEQ ID NOs:10-12, SEQ ID NOs:4-6, SEQ ID NOs:16-18 and SEQ ID NOs:13-15,~~ and satisfy the criteria of having both a frequency of CpG dinucleotides corresponding to an Observed/Expected Ratio >0.6, and a GC Content >0.5.

11. (Currently amended) The method of claim 1, wherein the cancer or cancer-related condition is selected from the group consisting of ~~gastrointestinal or~~ esophageal adenocarcinoma, ~~gastrointestinal or~~ esophageal dysplasia, ~~gastrointestinal or~~ esophageal metaplasia, Barrett's intestinal tissue, pre-cancerous conditions in normal esophageal squamous mucosa, and combinations thereof.

12. (Original) The method of claim 11, wherein the cancer is esophageal adenocarcinoma, and wherein making a diagnostic or prognostic prediction of the cancer, based upon the methylation state of the genomic CpG sequences provides for classification of the adenocarcinoma by grade or stage.

13. (Currently amended) The method of claim 6, wherein the cancer or cancer-related condition is selected from the group consisting of ~~gastrointestinal or~~ esophageal adenocarcinoma, ~~gastrointestinal or~~ esophageal dysplasia, ~~gastrointestinal or~~ esophageal metaplasia, Barrett's

intestinal tissue, pre-cancerous conditions in normal esophageal squamous mucosa, and combinations thereof.

14. (Original) The method of claim 13, wherein the cancer is esophageal adenocarcinoma, and wherein making a diagnostic or prognostic prediction of the cancer, based upon the methylation state of the genomic CpG sequences provides for classification of the adenocarcinoma by grade or stage.

15. (Original) The method of claim 1, wherein the methylation assay used to determine the methylation state of genomic CpG sequences is selected from the group consisting of MethylLight™, MS-SNuPE, MSP, COBRA, MCA, and DMH, and combinations thereof.

16. (Original) The method of claim 6, wherein the methylation assay used to determine the methylation state of genomic CpG sequences is selected from the group consisting of MethylLight™, MS-SNuPE, MSP, COBRA, MCA and DMH, and combinations thereof.

17. (Currently amended) The method of claim 1, wherein the methylation assay used to determine the methylation state of the at least one genomic CpG sequence ~~sequences~~ is based, at least in part, on an array or microarray comprising CpG-containing sequences located within the MYOD1 gene ~~at least one gene sequence selected from the group consisting of APC, ARF, CALCA, CDH1, CDKN2A, CDKN2B, ESRI, GSTP1, HIC1, MGMT, MLH1, MYOD1, RBI, TGFBR2, THBS1, TIMP3, CTNNB1, PTGS2, TYMS and MTHFR.~~

18. (Currently amended) The method of claim 17, wherein the MYOD1 gene sequence corresponds ~~corresponds~~ APC, ARF, CALCA, CDH1, CDKN2A, CDKN2B, ESRI, GSTP1, HIC1, MGMT, MLH1, MYOD1, RBI, TGFBR2, THBS1, TIMP3, CTNNB1, PTGS2, and TYMS gene sequences ~~correspond~~ to any CpG island sequences associated with the sequences defined by the specific oligonucleotide primers and probes corresponding to SEQ ID NOS:7-9 ~~SEQ ID NOS:1-54, 58-60, 64 and 65~~, as listed in TABLE II, or portions thereof, and wherein the associated CpG island sequences are those contiguous sequences of genomic DNA that encompass at least one nucleotide of the sequences defined by the specific oligonucleotide primers and probes corresponding to SEQ

ID NOS:7-9 ~~SEQ ID NOS:1-54, 58-60, 64 and 65~~, and satisfy the criteria of having both a frequency of CpG dinucleotides corresponding to an Observed/Expected Ratio >0.6, and a GC Content >0.5.

19. (Currently amended) The method of claim 17, wherein the MYOD1 gene sequence is ~~APC, ARF, CALCA, CDH1, CDKN2A, CDKN2B, ESR1, GSTP1, HIC1, MGMT, MLH1, MYOD1, RB1, TGFBR2, THBS1, TIMP3, CTNNB1, PTGS2, TYMS and MTHFR gene sequences~~ are those defined by, or correspond to the specific oligonucleotide primers and probes corresponding to ~~SEQ ID NOS:7-9~~ ~~SEQ ID NOS:1-60, 64 and 65~~, as listed in TABLE II, or portions thereof.

20. (Original) The method of claim 1 wherein the methylation state of genomic CpG sequences that is determined is that of hypermethylation, hypomethylation or normal methylation.

21. (Original) A kit useful for diagnosis or prognosis of cancer or cancer-related conditions, comprising a carrier means containing one or more containers comprising:

(a) a container containing a probe or primer which hybridizes to any region of a sequence located within at least one gene sequence selected from the group consisting of *APC*, *ARF*, *CALCA*, *CDH1*, *CDKN2A*, *CDKN2B*, *ESR1*, *GSTP1*, *HIC1*, *MGMT*, *MLH1*, *MYOD1*, *RB1*, *TGFBR2*, *THBS1*, *TIMP3*, *CTNNB1*, *PTGS2*, *TYMS* and *MTHFR*; and

(b) additional standard methylation assay reagents required to affect detection of methylated CpG-containing nucleic acid based, at least in part, on the probe or primer.

22. (Original) The kit of claim 21, wherein the additional standard methylation assay reagents are standard reagents for performing a methylation assay from the group consisting of MethyLight™, MS-SNuPE, MSP, COBRA, MCA and DMH, and combinations thereof.

23. (Original) The kit of claim 21, wherein the probe or primer comprises at least about 12 to 15 nucleotides of a sequence selected from the group consisting of SEQ ID NOS:1-60, 64 and 65, as listed in TABLE II.

24. (Original) A kit useful for diagnosis or prognosis of cancer or cancer-related conditions, comprising a carrier means containing one or more containers comprising:

(a) an array or micorarray comprising sequences of at least about 12 to 15 nucleotides of a sequence selected from the group consisting of SEQ ID NOs:1-60, 64, 65, and any sequence located within a CpG island sequence associated with SEQ ID NOs:1-54, 58-60, 64 and 65.